

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Histaclar 10mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 10 mg loratadine.

Excipient with known effect: each tablet contains 84.5 mg lactose monohydrate. For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White, round, biconvex film-coated tablets scored on one side and marked “LR 10” on the other side.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Histaclar Tablets are indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticaria in adults and children over the age of 2 years with a body weight more than 30 kg.

4.2 Posology and method of administration

Posology

Adults and children over 12 years of age:

10 mg once daily (one film-coated tablet once daily).

Paediatric population

Children 2 to 12 years of age *are dosed by weight*:

Body weight more than 30 kg:

10mg once daily (one film-coated tablet once daily).

Body weight 30 kg or less:

The 10 mg strength film-coated tablet is not appropriate in children with a body weight less than 30 kg.

Safety and efficacy of loratadine in children under 2 years of age has not been established. No data are available.

Patients with hepatic impairment

Patients with severe liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine. An initial dose of 10 mg every other day is recommended for adults and children weighing more than 30 kg.

Patients with renal impairment

No dosage adjustments are required in patients with renal insufficiency.

Elderly

No dosage adjustments are required in the elderly.

Method of administration

For oral use. The tablet may be taken without regard to mealtime.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Loratadine should be administered with caution in patients with severe liver impairment (see section 4.2).

Loratadine contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

The administration of loratadine should be discontinued at least 48 hours before skin tests since antihistamines may prevent or reduce otherwise positive reactions to dermal reactivity index.

4.5 Interaction with other medicinal products and other forms of interaction

When administered concomitantly with alcohol loratadine has no potentiating effects as measured by psychomotor performance studies.

Potential interaction may occur with all known inhibitors of CYP3A4 or CYP2D6 resulting in elevated levels of loratadine (see section 5.2), which may cause an increase in adverse events.

Increase in plasma concentrations of loratadine has been reported after concomitant use with ketoconazole, erythromycin, and cimetidine in controlled trials, but without clinically significant changes (including electrocardiographic).

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

A large amount of data on pregnant women (more than 1000 exposed outcomes) indicate no malformative nor foeto/neonatal toxicity of loratadine. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of loratadine during pregnancy.

Breast-feeding

Loratadine is excreted in breast milk. A risk to the newborns/infants cannot be excluded. The use of loratadine is not recommended in breast-feeding women.

Fertility

There are no data available on male and female fertility.

4.7 Effects on ability to drive and use machines

In clinical trials that assessed driving ability, no impairment occurred in patients receiving loratadine. However, patients should be informed that very rarely some people experience drowsiness, which may affect their ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

In clinical trials involving adults and adolescents in a range of indications including allergic rhinitis (AR) and chronic idiopathic urticaria (CIU), at the recommended dose of 10 mg daily, adverse reactions with loratadine were reported in 2% of patients in excess of those with placebo. The most frequent adverse reactions reported in excess of placebo were somnolence (1.2%), headache (0.6%), increased appetite (0.5%) and insomnia (0.1%). Other adverse reactions reported very rarely during the post-marketing period are listed in the following table by System Organ Class.

Tabulated list of adverse reactions

Frequencies are defined as very common ($\geq 1/10$), common ($\geq 1/100$ to $<1/10$), uncommon ($\geq 1/1,000$ to $<1/100$), rare ($\geq 1/10,000$ to $<1/1,000$), very rare ($<1/10,000$) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

<u>System Organ Classes</u>	<u>Common</u>	<u>Uncommon</u>	<u>Rare</u>	<u>Very Rare</u>
<u>Immune system disorders</u>				<u>Hypersensitivity reactions (including angioedema and anaphylaxis)</u>
<u>Nervous system disorders</u>				<u>Dizziness, convulsion</u>
<u>Cardiac disorders</u>				<u>Tachycardia, palpitation</u>
<u>Gastrointestinal disorders</u>				<u>Nausea, dry mouth, gastritis</u>
<u>Hepatobiliary disorders</u>				<u>Abnormal hepatic function</u>
<u>Skin and subcutaneous tissue disorders</u>				<u>Rash, alopecia</u>
<u>General disorders and administration site conditions</u>				<u>Fatigue</u>

Paediatric population

In clinical trials in a paediatric population, children aged 2 through 12 years, common adverse reactions reported in excess of placebo were headache (2.7%), nervousness (2.3%), and fatigue (1%).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: <http://www.hpra.ie/>; E-mail: medsafety@hpra.ie.

4.9 Overdose

Overdosage with loratadine increased the occurrence of anticholinergic symptoms. Somnolence, tachycardia, and headache have been reported with overdoses.

In the event of overdose, general symptomatic and supportive measures are to be instituted and maintained for as long as necessary. Administration of activated charcoal as a slurry with water may be attempted. Gastric lavage may be

considered. Loratadine is not removed by haemodialysis and it is not known if loratadine is removed by peritoneal dialysis. Medical monitoring of the patient is to be continued after emergency treatment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antihistamines for systemic use,
ATC code: R06AX13.

Mechanism of action

Loratadine, the active ingredient in Histaclar tablets, is a tricyclic antihistamine with selective, peripheral H₁-receptor activity.

Pharmacodynamic effects

Loratadine has no clinically significant sedative or anticholinergic properties in the majority of the population and when used at the recommended dosage.

During long-term treatment there were no clinically significant changes in vital signs, laboratory test values, physical examinations or electrocardiograms.

Loratadine has no significant H₂-receptor activity. It does not inhibit norepinephrine uptake and has practically no influence on cardiovascular function or no intrinsic cardiac pacemaker activity.

Human histamine skin wheal studies following a single 10 mg dose has shown that the antihistamine effects are seen within 1-3 hours reaching a peak at 8-12 hours and lasting in excess of 24 hours. There was no evidence of tolerance to this effect after 28 days of dosing with loratadine.

Clinical efficacy and safety

Over 10,000 subjects (12 years and older) have been treated with loratadine 10 mg tablets in controlled clinical trials. Loratadine 10 mg tablets once daily was superior to placebo and similar to clemastine in improving the effects on nasal and non-nasal symptoms of AR. In these studies somnolence occurred less frequently with loratadine than with clemastine and about the same frequency as terfenadine and placebo.

Among these subjects (12 years and older), 1000 subjects with CIU were enrolled in placebo controlled studies. A once daily 10 mg dose of loratadine was superior to placebo in the management of CIU as demonstrated by the reduction of associated itching, erythema and hives. In these studies the incidence of somnolence with loratadine was similar to placebo.

Paediatric population

Approximately 200 paediatric subjects (6 to 12 years of age) with seasonal allergic rhinitis received doses of loratadine syrup up to 10 mg once daily in controlled clinical trials. In another study, 60 paediatric subjects (2 to 5 years of age) received 5 mg of loratadine syrup once daily. No unexpected adverse events were observed.

The paediatric efficacy was similar to the efficacy observed in adults.

5.2 Pharmacokinetic properties

Absorption

Loratadine is rapidly and well-absorbed. Concomitant ingestion of food can delay slightly the absorption of loratadine but without influencing the clinical effect.

The bioavailability parameters of loratadine and of the active metabolite are dose proportional.

Distribution

Loratadine is highly bound (97% - 99 %) and its active major metabolite desloratadine (DL) moderately bound (73% -

76%) to plasma proteins.

In healthy subjects, plasma distribution half-lives of loratadine and its active metabolite are approximately 1 and 2 hours, respectively.

Biotransformation

After oral administration, loratadine is rapidly and well absorbed and undergoes an extensive first pass metabolism, mainly by CYP3A4 and CYP2D6. The major metabolite - desloratadine (DL) is pharmacologically active and responsible for a large part of the clinical effect. Loratadine and DL achieve maximum plasma concentrations (t_{\max}) between 1 - 1.5 hours, and 1.5 - 3.7 hours after administration, respectively.

Elimination

Approximately 40 % of the dose is excreted in the urine and 42% in the faeces over a 10 day period and mainly in the form of conjugated metabolites. Approximately 27% of the dose is eliminated in the urine during the first 24 hours. Less than 1% of the active substance is excreted unchanged in the active form, as loratadine or DL.

The mean elimination half-lives in healthy adult subjects were 8.4 hours (range = 3 to 20 hours) for loratadine and 28 hours (range = 8.8 to 92 hours) for the major active metabolite.

Renal impairment

In patients with chronic renal impairment, both the AUC and peak plasma levels (C_{\max}) increased for loratadine and its metabolite as compared to the AUCs and peak plasma levels (C_{\max}) of patients with normal renal function. The mean elimination half-lives of loratadine and its metabolite were not significantly different from that observed in normal subjects. Haemodialysis does not have an effect on the pharmacokinetics of loratadine or its active metabolite in subjects with chronic renal impairment.

Hepatic impairment

In patients with chronic alcoholic liver disease, the AUC and peak plasma levels (C_{\max}) of loratadine were doubled while the pharmacokinetic profile of the active metabolite was not significantly changed from that in patients with normal liver function. The elimination half-lives for loratadine and its metabolite were 24 hours and 37 hours, respectively, and increased with increasing severity of liver disease.

Elderly

The pharmacokinetic profile of loratadine and its active metabolite is comparable in healthy volunteers and in healthy geriatric volunteers.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, and carcinogenic potential.

In reproductive toxicity studies, no teratogenic effects were observed. However, prolonged parturition and reduced viability of offspring were observed in rats at plasma levels (AUC) 10 times higher than those achieved with clinical doses.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Lactose monohydrate
Cellulose, microcrystalline
Maize starch
Starch, pregelatinised

Silica colloidal hydrated
Magnesium stearate

Film-coat
Hypromellose
Macrogol 400 and 6000
Carnauba wax
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in the original package.

6.5 Nature and contents of container

PVC/Aluminium blister packs.

Blister pack sizes of 5, 7, 10, 14, 15, 20, 21, 30, 50 and 100.
Not all pack sizes will be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

McDermott Laboratories
T/A Gerard Laboratories
35/36 Baldoyle Industrial Estate
Grange Road
Dublin 13
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 0577/046/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of last authorisation: 24 January 2003

Date of last renewal: 01 August 2006

10 DATE OF REVISION OF THE TEXT

July 2015